UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,108	01/15/2002	Stein Ove Doskeland	Q-64374	8288

7590 10/11/2006

Sughrue Mion Zinn Macpeak & Seas
2100 Pennsylvania Avenue N W
Washington, DC 20037-3213

EXAMINER	
YANG, NELSON C	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,108	DOSKELAND ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-8,10-14,21 and 23-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8, 10-14, 21, 23-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 2-8, 10-14, 21, 23-27 are currently pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 2-8, 10-14, 21, 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al [US 4,554,088] in view of Ward et al [Ward et al, Colorimetric protein phosphatase inhibition assay of laboratory strains and natural blooms of cyanobacteria: comparisons with high performance liquid chromatographic analysis for microcystins, 1997, FEMS Microbiology Letters, 153, 465-473].

With respect to claim 21, Whitehead et al. teach a method for isolation of molecules by placing selective bioaffinity adsorbents (first ligand) on magnetic particles to which labeled ligates (second ligand) and nonlabeled ligates will bind, separating the bound ligates from free ligates, and the label measured (column 15, lines 1-45). Whitehead et al. further teach that the ligand /ligates may include enzyme/inhibitors (column 7, lines 25-35, column 17, Table III). Whitehead et al. also teach that this enables the efficient isolation of molecules (column 17, lines 16-25). While Whitehead et al. teaches a generic assay for the detection of inhibitors of enzymes,

Whitehead et al. fail to specifically teach an assay for an inhibitor is a phosphatase-targeting toxin involving the use of protein phosphatase.

Ward et al, however, teach a colorimetric protein phosphatase inhibition assay for microcystins using protein phosphatases (p.467, col. 1). Ward et al further teach that microcystins are a group of cyclic heptapeptide hepatotxins capable of being produced by common bloom-forming genera of cyanobacteria (p.465, col.1), and which bind irreversibly to and inhibit protein phosphatases 1 and 2A (p.465, col.2). Ward et al further teach that due to the increased awareness of the hazards presented by these toxins, increasingly sensitive detection methods are required to provide information for the effective management of waters supporting cyanobacterial blooms (p.466, col.1, pg.2).

Therefore, it would have been obvious to one of ordinary skill in the art to have utilized the method of Whitehead et al to detect specific inhibitors such as microcystins, as suggested by Ward et al, by using an enzyme such as a protein phosphatase as the bioaffinity adsorbent, because the method of Whitehead et al is generic with respect to the analytes that can be detected and the specific binding reagents that can be used and would be motivated to use the appropriate reagents (protein phosphatases) to detect the desired analyte (microcystins), in the method of Whitehead et al., who further teach that the method allows for the efficient isolation of molecules.

4. With respect to claims 2-3, Ward et al teach that microcystins are a group of cyclic heptapeptide hepatotxins capable of being produced by common bloom-forming genera of cyanobacteria (p.465, col.1),

5. With respect to claims 4, 11, Whitehead et al teach that the labeled ligate and nonlabeled ligates compete for binding to the ligand (column 15, lines 28-45). Since Ward et al teach the use of protein phosphatases as the enzymes to detect toxins such as microcystins (p.466, col.1, pgs.2-3), the labeled ligate and nonlabeled ligates would be labeled and nonlabeled microcystins, which are heptapeptide hepatotoxins.

6. With respect to claim 5, Whitehead et al teach that the amount of unlabeled ligand (toxin) can be determined by collecting the ligand-labeled ligand complex and measuring the label, and using a standard curve to determine the amount of unlabeled ligate (toxin) (column 15, liens 35-40).

7. With respect to claim 6, Ward et al suggests that the detection methods are used for potable waters (p. 466, col.1, pg. 2).

8. With respect to claim 7, Whitehead et al teach that the ligates may include antibodies (column 17, liens 45-60).

9. With respect to claim 8, Whitehead et al teach that microcystins bind irreversibly to and inhibit protein phosphatases 1 and 2A (p. 465, col.2), demonstrating that PP1 and PP2A are equivalent structures known in the art. Therefore, because these two were art-recognized equivalents at the time the invention was made, one of ordinary skill in the art would have found it obvious to substitute for

10. With respect to claim 10, Whitehead et al teach labeled ligate (second ligand) (column 15, lines 10-15) which would contain a label (reporter moiety).

11. With respect to claim 12, the microcystins to be detected include microcystin-LR (p.465, col.2).

12. With respect to claim 13, Whitehead et al teach ligands coupled to an insoluble support or matrix (column 17, lines 20-30).

13. With respect to claim 14, Whitehead et al teach magnetic particles (column 7, lines 5-15).

14. With respect to claims 23-24, Whitehead et al teach that the bioaffinity adsorbents are bound to the particles covalently (column 7, lines 36-45) or through silane linkages (column 7, lines 45-55).

15. With respect to claim 25, Whitehead et al teach that the labeled ligate is measured directly (column 15, lines 38-40).

16. With respect to claim 26, Whitehead et al teach that competitive assays may be run with labeled ligand and unlabeled ligate (second ligand) (column 15, lines 11-15), which would result in the unlabeled ligate being determined indirectly.

17. With respect to claim 27, Whitehead et al teach competitive assays in which the amount of bound measaurable label is inversely proportional to the amount of analyte in solution (column 8, lines 25-40).

Response to Arguments

18. Applicant's arguments filed July 13, 2006 have been fully considered but they are not persuasive.

19. Applicant's arguments that Ward et al. was published well after Whitehead et al. and despite being armed with the knowledge of Whitehead et al. and the fact that the techniques of Whitehead were well known and commercially available well before 1997, did not teach or suggest the binding assay as presently claimed are not found persuasive. In response to applicant's argument based upon the age of the references, contentions that the reference patents

are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977). In particular, since the reference of Ward et al. does not teach that the techniques of Whitehead et al. would not work in detection of a phosphatase targeting toxin, it does not teach away from the combination of the invention as disclosed above in the 103(a) rejection, and one of ordinary skill in the art would have had a reasonable expectation of success

20. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one would be motivated to use the appropriate reagents (protein phosphatases) to detect the desired analyte (microcystins) in order to obtain detection methods that provide information for the effective management of waters supporting cyanobacterial blooms (p.466, col.1, pg.2).

21. Furthermore, it should be noted that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In

particular, since Whitehead et al. substantially discloses the method of the invention for detecting enzyme inhibitors using enzymes, and Ward et al. discloses the need for detecting microcystins, inhibitors, using protein phosphatases, an enzyme, on of ordinary skill in the art would have been motivated to use protein phosphatases in the method of Whitehead et al. to detect inhibitors such as microcystins.

22. Although applicant has provided a different reason for performing the method as claimed (see p. 3, 11), i.e., that the method of the present invention is less susceptible to interfering factors, when compared to protein phosphatase enzyme inhibition assays, and allows determination of the toxicity of the sample based upon the level of physiological toxins, as opposed to ELISA assays, which do not accurately reflect sample toxicity, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

23. With respect to applicant's arguments that there exists a long felt need in the art, the Office does not dispute this fact, nor the fact that the invention as claimed by applicants may address this need. However, it should be noted that in some of the references, such as with Sikorska [US 5,264,556], the prior art discloses a method that presumably address this long felt need as well.

24. With respect to applicant's arguments that the present invention is superior to both protein phosphatase enzyme inhibition assays and ELISA assays, the Office notes applicant's assertion. If Whitehead et al. had merely disclosed using an antibody to detect the presence of the

toxin, or had not taught the use of enzymes immobilized to a support, this would have been found persuasive.

However, the Office notes that the method of Whitehead et al. discloses applicant's method as recited with the exception that Whitehead et al. merely disclose that the method utilizes an enzyme for detecting an inhibitor, and do not disclose a specific enzyme (protein phosphatase) for detecting a specific inhibitor (hepatotoxins). Ward et al. provides the motivation for having the specific enzyme, protein phosphatase, for detecting microcystins (a hepatotoxin), as discussed above, (sensitive detection methods for providing information for the effective management of waters supporting cyanobacterial blooms). Therefore, applicant's argument is not found persuasive

25. With respect to applicant's citation of Holmes [US 5,180,665] (see p.6, bottom), the Office notes that applicants do not recite testing a crude sample, and so does not see how the citation would necessarily be relevant to the rejections made. However, if applicants intend to argue that one of ordinary skill in the art would not have had a reasonable expectation of success in using protein phosphatase enzymes to detect inhibitors such as phosphatase targeting toxins in the method of Whitehead et al., or that the applicants discovered unexpected results, applicants may wish to further expand on the reasons why. In particular, applicants may wish to provide art that has disclosed that one would not have expected the combination to work, or by other forms of evidence.

26. For these reasons, the rejections has been maintained.

Conclusion

27. No claims are allowed.

28. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

30. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Nelson Yang
Patent Examiner
Art Unit 1641

LONG V. LE 04/29/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600